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L34 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:634046 HCAPLUS

DOCUMENT NUMBER: 141:167820

TITLE: Brain progenitor cell division-modulating agent assay, and related therapeutic methods and compositions

INVENTOR(S): Hen, Rene; Santarelli, Luca; Saxe, Michael

PATENT ASSIGNEE(S): The Trustees of Columbia University In the City of New York, USA

SOURCE: PCT Int. Appl., 97 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004065567	A2	20040805	WO 2004 US1751	20040122
W:	AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI			
US 2004247525	A1	20041209	US 2004-764068	20040122
PRIORITY APPLN. INFO.:			US 2003-442081P	P 20030123
			US 2003-526190P	P 20031201

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides methods for determining whether an agent increases brain progenitor cell division in a subject. The invention also provides methods for treating anxiety, depression, a cognitive disorder or a neurodegenerative disorder or inhibiting the onset of anxiety, depression or a cognitive disorder by administering to an afflicted subject a therapeutically or prophylactically effective amount of the agent. The invention further provides methods for treating anxiety, depression, cognitive disorder or a neurodegenerative disorder or inhibiting the onset of anxiety, depression or a cognitive disorder by administering to an afflicted subject a therapeutically or prophylactically effective amount of Hh-Ag 1.1 (I), Hh-Ag 1.2 (II), Hh-Ag 1.3 (III), or derivs. thereof.

IT 150428-23-2, Cyclin-dependent kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (brain progenitor cell division-modulating agent assay, and related therapeutic methods and compns.)

RN 150428-23-2 HCAPLUS

CN Kinase (phosphorylating), protein (cyclin-dependent) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 140084-69-1, GENBANK X58708 173079-18-0, GENBANK X82786 216478-43-2, GENBANK AF089721 221020-55-9, GENBANK

AF105292 225914-56-7, GENBANK AF151353 384408-02-0,
GENBANK AB073819 384493-30-5, GENBANK M90364 384583-93-1
, GENBANK U09968 391543-98-9, GENBANK L12029 391546-44-4
, GENBANK X75888 418503-00-1, GENBANK AF488732
419496-59-6, GENBANK AY057907 466622-99-1, GENBANK
AF533752 496198-28-8, GENBANK BC044841 523335-95-7,
GENBANK BC052434

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(brain progenitor cell division-modulating agent assay, and related
therapeutic methods and comps.)

RN 140084-69-1 HCAPLUS
CN DNA, (mouse clone pC5237 gene cycB cyclin B cDNA plus flanks) (9CI) (CA
INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 173079-18-0 HCAPLUS
CN DNA (mouse clone TSG126.1 proliferation antigen Ki-67 cDNA plus flanks)
(9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 216478-43-2 HCAPLUS
CN DNA (mouse gene SMOH 3'-UTR (untranslated region) fragment-specifying
cDNA) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 221020-55-9 HCAPLUS
CN DNA (Mus musculus strain A p75NGFR (receptor) cDNA plus flanks) (9CI) (CA
INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 225914-56-7 HCAPLUS
CN GenBank AF151353 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 384408-02-0 HCAPLUS
CN DNA (mouse gene Wnt14b glycoprotein cDNA plus flanks) (9CI) (CA INDEX
NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 384493-30-5 HCAPLUS
CN GenBank M90364 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 384583-93-1 HCAPLUS
CN GenBank U09968 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 391543-98-9 HCAPLUS
CN DNA (mouse cell line ST-2 gene SDF-1-alpha cDNA) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 391546-44-4 HCAPLUS
CN GenBank X75888 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 418503-00-1 HCAPLUS
CN GenBank AF488732 (9CI) (CA INDEX NAME)

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RN 419496-59-6 HCAPLUS
CN GenBank AY057907 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 466622-99-1 HCAPLUS
CN DNA (mouse strain Swiss Webster gene Aspm protein fragment-specifying cDNA) (9CI) (CA INDEX NAME)

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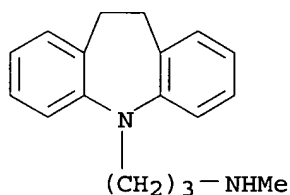
RN 496198-28-8 HCAPLUS
CN DNA (mouse strain 129,C57BL/6J,FVB/N clone MGC:7003 IMAGE:3155470 Ccnd1 protein cDNA) (9CI) (CA INDEX NAME)

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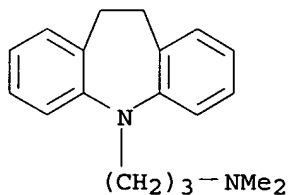
RN 523335-95-7 HCAPLUS
CN DNA (mouse strain C57BL/6 clone MGC:63392 IMAGE:6837113 Cdc6 protein cDNA) (9CI) (CA INDEX NAME)

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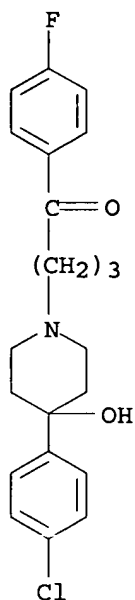
IT 50-47-5, Desipramine 50-49-7, Imipramine 52-86-8
, Haloperidol 54910-89-3, Fluoxetine
RL: PAC (Pharmacological activity); BIOL (Biological study)
(brain progenitor cell division-modulating agent assay, and related therapeutic methods and compns.)
RN 50-47-5 HCAPLUS
CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N-methyl- (9CI) (CA INDEX NAME)



RN 50-49-7 HCAPLUS
CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

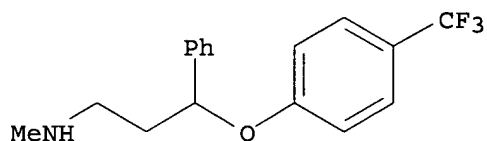


RN 52-86-8 HCAPLUS
CN 1-Butanone, 4-[4-(4-chlorophenyl)-4-hydroxy-1-piperidinyl]-1-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



RN 54910-89-3 HCAPLUS

CN Benzenepropanamine, N-methyl-γ-[4-(trifluoromethyl)phenoxy]- (9CI)
(CA INDEX NAME)

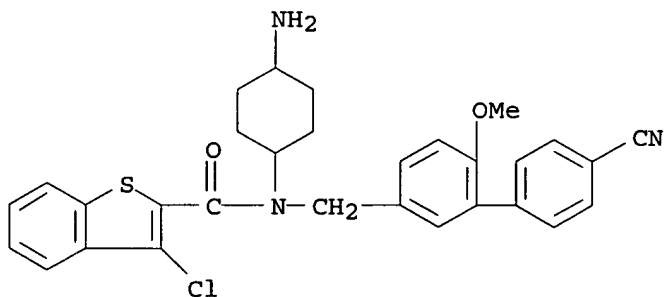


IT 364590-52-3 364590-52-3D, derivs. 364590-54-5
364590-54-5D, derivs. 364590-63-6 364590-63-6D
, derivs.

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(brain progenitor cell division-modulating agent assay, and related
therapeutic methods and compns.)

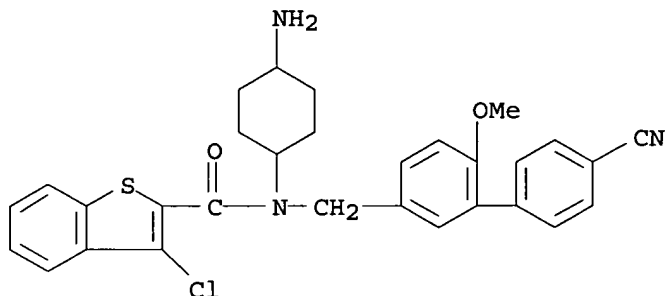
RN 364590-52-3 HCAPLUS

CN Benzo[b]thiophene-2-carboxamide, N-(4-aminocyclohexyl)-3-chloro-N-[(4'-
cyano-6-methoxy[1,1'-biphenyl]-3-yl)methyl]- (9CI) (CA INDEX NAME)



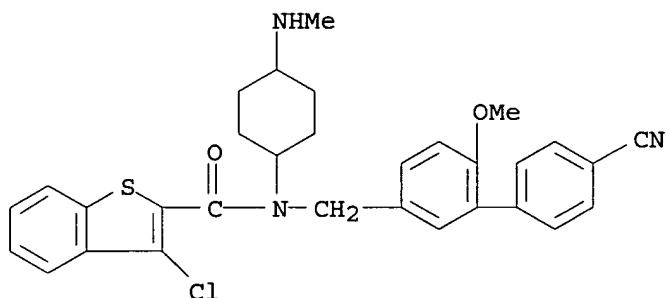
RN 364590-52-3 HCAPLUS

CN Benzo[b]thiophene-2-carboxamide, N-(4-aminocyclohexyl)-3-chloro-N-[(4'-cyano-6-methoxy[1,1'-biphenyl]-3-yl)methyl]- (9CI) (CA INDEX NAME)



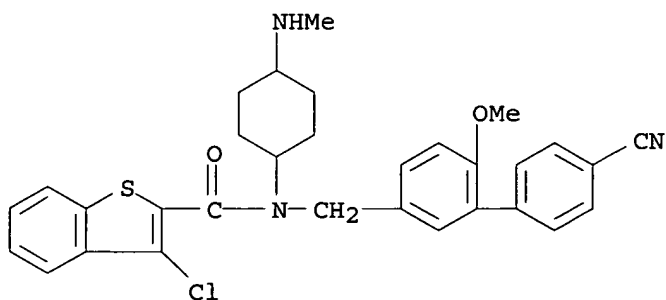
RN 364590-54-5 HCAPLUS

CN Benzo[b]thiophene-2-carboxamide, 3-chloro-N-[(4'-cyano-6-methoxy[1,1'-biphenyl]-3-yl)methyl]-N-[4-(methylamino)cyclohexyl]- (9CI) (CA INDEX NAME)



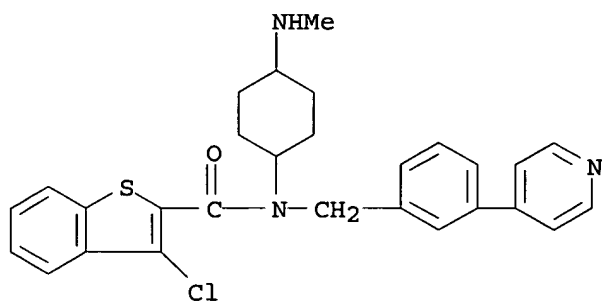
RN 364590-54-5 HCAPLUS

CN Benzo[b]thiophene-2-carboxamide, 3-chloro-N-[(4'-cyano-6-methoxy[1,1'-biphenyl]-3-yl)methyl]-N-[4-(methylamino)cyclohexyl]- (9CI) (CA INDEX NAME)



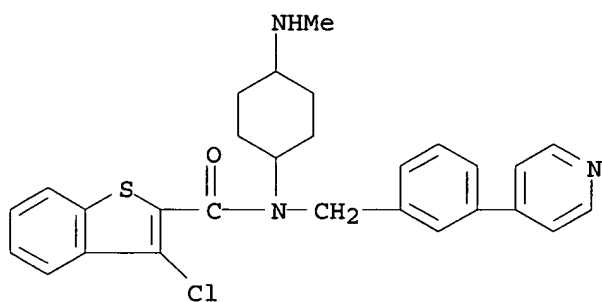
RN 364590-63-6 HCAPLUS

CN Benzo[b]thiophene-2-carboxamide, 3-chloro-N-[4-(methylamino)cyclohexyl]-N-[[3-(4-pyridinyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 364590-63-6 HCAPLUS

CN Benzo[b]thiophene-2-carboxamide, 3-chloro-N-[4-(methylamino)cyclohexyl]-N-[[3-(4-pyridinyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



IT 9001-66-5, Monoamine oxidase 9025-82-5,

Phosphodiesterase 443900-95-6, GSK3 β

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; brain progenitor cell division-modulating agent assay, and
related therapeutic methods and compns.)

RN 9001-66-5 HCAPLUS

CN Oxidase, monoamine (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9025-82-5 HCAPLUS

CN Phosphodiesterase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 443900-95-6 HCAPLUS

CN Kinase (phosphorylating), protein, GSK3 β (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

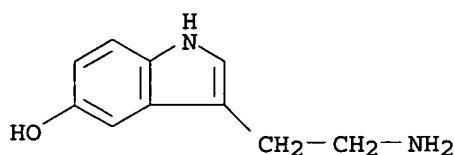
IT 50-67-9, Serotonin, biological studies 51-41-2,

Norepinephrine

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(selective uptake inhibitors; brain progenitor cell division-modulating
agent assay, and related therapeutic methods and compns.)

RN 50-67-9 HCAPLUS

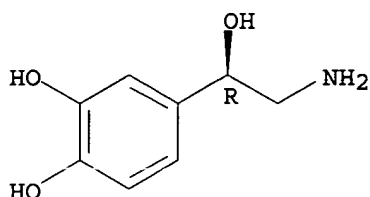
CN 1H-Indol-5-ol, 3-(2-aminoethyl)- (9CI) (CA INDEX NAME)



RN 51-41-2 HCAPLUS

CN 1,2-Benzenediol, 4-[(1R)-2-amino-1-hydroxyethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L34 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:284185 HCAPLUS

DOCUMENT NUMBER: 140:354554

TITLE: The serotonergic system and anxiety

AUTHOR(S): Gordon, Joshua A.; **Hen, Rene**

CORPORATE SOURCE: Department of Psychiatry, Center for Neurobiology and Behavior, New York State Psychiatric Institute, Columbia University, USA

SOURCE: NeuroMolecular Medicine (2004), 5(1), 27-40

CODEN: NMEEAN; ISSN: 1535-1084

PUBLISHER: Humana Press Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

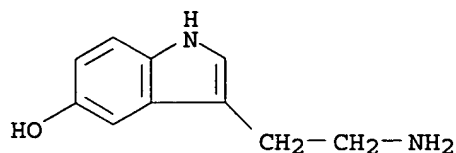
AB A review. The wide use of serotonin reuptake inhibitors and serotonin receptor agonists in anxiety disorders has suggested a key role for the modulatory neurotransmitter in anxiety. However, serotonin's specific role is still uncertain. This article reviews the literature concerning how and where serotonergic agents modulate anxiety. Varying and sometimes conflicting data from human and animal studies argue for both anxiolytic and anxiogenic roles for serotonin, depending on the specific disorder, structure, or behavioral task studied. However, recent data from molecular genetic studies in the mouse point toward two important roles for the serotonin 1A receptor. In development, serotonin acts through this receptor to promote development of the circuitry necessary for normal anxiety-like behaviors. In adulthood, serotonin reuptake inhibitors act through the same receptor to stimulate **neurogenesis** and reduce anxiety-like behaviors. These studies highlight that the complex serotonin system likely plays various roles in the regulation of anxiety both during development and in adulthood.

IT 50-67-9, Serotonin, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(serotonergic agents and anxiety)

RN 50-67-9 HCAPLUS

CN 1H-Indol-5-ol, 3-(2-aminoethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 108 THERE ARE 108 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:605908 HCAPLUS

DOCUMENT NUMBER: 139:255212

TITLE: Requirement of Hippocampal **Neurogenesis** for the Behavioral Effects of Antidepressants

AUTHOR(S): **Santarelli, Luca; Saxe, Michael;**
Gross, Cornelius; Surget, Alexandre; Battaglia, Fortunato; Dulawa, Stephanie; Weisstaub, Noelia; Lee, James; Duman, Ronald; Arancio, Ottavio; Belzung, Catherine; **Hen, Rene**

CORPORATE SOURCE: Center for Neurobiology and Behavior, Columbia University, New York, NY, 10032, USA

SOURCE: Science (Washington, DC, United States) (2003), 301(5634), 805-809

CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science

DOCUMENT TYPE: Journal

LANGUAGE: English

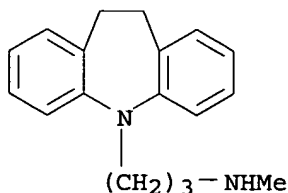
AB Various chronic antidepressant treatments increase adult hippocampal **neurogenesis**, but the functional importance of this phenomenon remains unclear. Here, using genetic and radiol. methods, we show that disrupting antidepressant-induced **neurogenesis** blocks behavioral responses to antidepressants. Serotonin 1A receptor null mice were insensitive to the **neurogenic** and behavioral effects of fluoxetine, a serotonin selective reuptake inhibitor. X-irradiation of a restricted region of mouse brain containing the hippocampus prevented the **neurogenic** and behavioral effects of two classes of antidepressants. These findings suggest that the behavioral effects of chronic antidepressants may be mediated by the stimulation of **neurogenesis** in the hippocampus.

IT 50-47-5, Desipramine 50-49-7, Imipramine 52-86-8, Haloperidol 54910-89-3, Fluoxetine

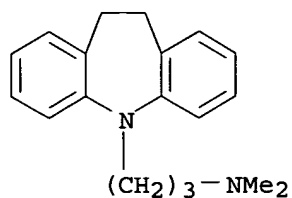
RL: DMA (Drug mechanism of action); BIOL (Biological study) (requirement of hippocampal **neurogenesis** for behavioral effects of antidepressants)

RN 50-47-5 HCAPLUS

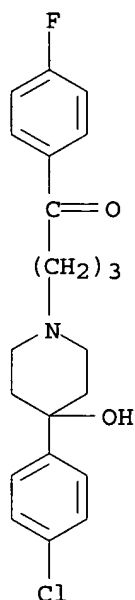
CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N-methyl- (9CI) (CA INDEX NAME)



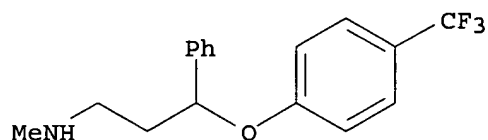
RN 50-49-7 HCAPLUS
CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N-dimethyl- (9CI)
(CA INDEX NAME)



RN 52-86-8 HCAPLUS
CN 1-Butanone, 4-[4-(4-chlorophenyl)-4-hydroxy-1-piperidinyl]-1-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



RN 54910-89-3 HCAPLUS
CN Benzenepropanamine, N-methyl-γ-[4-(trifluoromethyl)phenoxy]- (9CI)
(CA INDEX NAME)



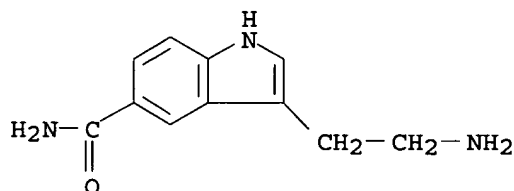
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:64267 HCAPLUS

DOCUMENT NUMBER: 130:262485
TITLE: Putative 5-HT5 receptors: localization in the mouse
CNS and lack of effect in the inhibition of dural
protein extravasation
AUTHOR(S): Waeber, C.; Grailhe, R.; Yu, X.-J.; Hen, R.;
Moskowitz, M. A.
CORPORATE SOURCE: Massachusetts General Hospital, Harvard Medical
School, Charlestown, MA, 02129, USA
SOURCE: Annals of the New York Academy of Sciences (1998),
861(Advances in Serotonin Receptor Research), 85-90
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Putative 5-ht5 receptor binding sites were visualized by in vitro autoradiog. using [125I]LSD (in the presence of clozapine and spiperone) or [3H]5-carboxamidotryptamine (in the presence 8-OH-DPAT, GR127935 and spiperone). Under these conditions, no [3H]5-carboxamidotryptamine labeling was detected in the brain of mice lacking the gene encoding the putative 5-ht5a receptor (knockout mice), whereas intermediate densities of binding sites were seen in the olfactory bulb and neocortex of wild-type mice. [125I]LSD labeled the same areas as [3H]5-carboxamidotryptamine in wild-type mice. High densities of [125I]LSD binding sites were observed in the medial habenula of wild type and knockout mice. 5-CT competed for [125I]LSD binding sites with an affinity of 2 nM in the olfactory bulb and neocortex of wild-type mice and an affinity of 30 nM in the habenula of knockout mice, suggesting that habenular labeling might be accounted for by putative 5-ht5b receptors. In the presence of 5'-guanylylimidodiphosphate, 5-CT displaced [125I]LSD from putative 5-ht5a and 5-ht5b sites with a 6-times and 3-times lower affinity, resp., suggesting that both receptor subtypes are coupled to G proteins in brain. We also studied the inhibitory effect of 5-CT on dural **neurogenic** inflammation in knockout mice. In wild type mice, 3 ng/kg 5-CT inhibited dural protein extravasation by 60 %. A similar effect was observed in knockout mice, even in the presence of the 5-HT1B receptor antagonist GR127935. These results suggest that the inhibitory effects of 5-CT are not mediated by a site with the characteristics of the putative 5-ht5 receptor.

IT 74885-09-9, 5-Carboxamidotryptamine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(putative 5-HT5 receptors, their localization in the mouse CNS and lack of effect in the inhibition of dural protein extravasation)
RN 74885-09-9 HCAPLUS
CN 1H-Indole-5-carboxamide, 3-(2-aminoethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT